

Non-Technical Abstract

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Multiple myeloma (MM) is a disease of tumor masses infiltrating the bone and bone marrow. The tumor originates in the bone marrow tissues that produce blood cells. The disease is usually progressive and generally fatal. The incidence of MM in the U.S. is 5 per 100,000; there were 12,800 new cases in 1993. The median age at diagnosis is 62 and it is more common in men than in women.

Transplantation of bone marrow from healthy donors (allo-BMT) is commonly used to treat MM patients. This can cure the disease; however, up to 50% of patients die as a result of rejecting the white blood cells (immune cells) in the donor's bone marrow. This is known as Graft-versus-Host disease (GVHD). To alleviate this problem allo-BMTs are given without T-cells (one of the immune cells) which causes a decrease in GVHD, however problems such as disease relapse, graft failure, and severe immune deficiency occur. Donor immune cells have been given to relapsed MM patients who have undergone an allo-BMT without T-cells. This standard therapy has been shown to produce complete disease remission, but GVHD still occurs.

In this experimental protocol donor immune cells will be administered to relapsed MM patients who have undergone an allo-BMT without T-cells. In order to manage the effects of GVHD, prior to administration the donor cells will be transduced with a retroviral vector containing the gene for thymidine kinase. In the event of GVHD, cells transduced with this vector can be killed by giving the patient infusions of the drug ganciclovir. These cells will also be transduced with a marker gene in the vector, which will allow us to study their role following infusion.

Patients will be monitored for MM disease remission as well as development of severe GVHD and infusions of transduced cells and ganciclovir will be administered accordingly. If severe GVHD does not develop and no decrease in disease is observed, the dose will be escalated five times (three patients per dose):  $1 \times 10^6$ ,  $5 \times 10^6$ ,  $1 \times 10^7$ ,  $2 \times 10^7$ , or  $5 \times 10^7$  transduced lymphocytes per kilogram.

The objectives of this study are to evaluate the:

- 1) Safety of transduced donor cell infusions.
- 2) Effectiveness of donor infusions in decreasing the effects of severe GVHD.
- 3) Effectiveness of donor infusions in MM disease remission.
- 4) Effectiveness of donor cell removal with ganciclovir in preventing the depletion of red blood cells.